

WHAT IS CLAIMED IS:

1. A method of identifying a candidate therapeutic compound for treating FSHD, the method comprising,

- (a) providing a D4Z4 binding element;
- (b) contacting the D4Z4 binding element with a test compound; and
- (c) determining whether the test compound interacts with the D4Z4 binding element,

wherein an interaction between the D4Z4 binding element and the test compound indicates that the test compound is a candidate therapeutic compound.

2. The method of claim 1, wherein the D4Z4 binding element is in a cell that expresses a 4q35 gene.

3. The method of claim 2, further comprising the step of determining the level of expression of a 4q35 gene compared to a reference.

4. The method of claim 3, wherein the 4q35 gene is FSHD region gene 1 (*FRG1*), FSHD region gene 2 (*FRG2*), or adenine nucleotide translocator-1 gene (*ANT1*).

5. The method of claim 1, wherein the cell is a muscle cell.

6. The method of claim 5, wherein the cell is from a subject that has FSHD.

7. The method of claim 1, wherein the interaction is the binding of the test compound to the D4Z4 binding element.

8. A method of identifying a candidate compound for treating FSHD, the method comprising,

- (a) providing a cell that can express a D4Z4 recognition complex component;
- (b) contacting the cell with a test compound; and

(c) measuring expression of the D4Z4 recognition complex component, wherein an increase in expression of the D4Z4 recognition complex component compared to a reference cell that was not contacted with the test compound indicates that the test compound is a candidate compound for treating FSHD.

8. The method of claim 8, wherein the D4Z4 recognition complex component is YY1, HMGB2, or nucleolin.

9. A method of identifying a candidate compound for treating FSHD, the method comprising,

- (a) providing a D4Z4 binding element (DBE) and a D4Z4 recognition complex (DRC) under conditions such that the DBE and the DRC can interact;
- (b) contacting the D4Z4 binding element and DRC or a DRC component with a test compound; and
- (c) determining whether the test compound affects the interaction between the D4Z4 binding element and the DRC or DRC component,

wherein an increase in the interaction between the D4Z4 binding element and the DRC or DRC component in the presence of the test compound indicates that the test compound is a candidate compound.

10. The method of claim 9, wherein the DRC component is YY1, HMGB2, or nucleolin.

11. A method of determining whether a treatment for FSHD is effective, the method comprising

- (a) obtaining a biological sample from a subject being treated for FSHD,
- (b) determining the level of expression of a 4q35 gene,

(c) comparing the level of expression of the 4q35 gene to a reference, wherein a decrease in the level of expression of the FSHD gene relative to a reference indicates that the FSHD treatment is effective.

12. The method of claim 11, wherein the 4q35 gene is FSHD region gene 1 (*FRG1*), FSHD region gene 2 (*FRG2*), or adenine nucleotide translocator-1 gene (*ANT1*).

13. The method of claim 11, wherein expression of at least two 4q35 genes is decreased in the biological sample.

14. A method of treating a subject having or at risk for FSHD, the method comprising administering to the subject a compound that increases the expression or activity of at least one component of a D4Z4 recognition complex (DRC).

15. The method of claim 14, wherein the component of the D4Z4 recognition complex is YY1, HMGB2, or nucleolin.

16. A method of identifying a subject having or at risk of having facioscapulohumeral muscular dystrophy (FSHD), the method comprising

- (a) obtaining a biological sample from the subject
- (b) determining the level of expression of a 4q35 gene in the sample
- (c) comparing the level of expression of the 4q35 gene in the sample compared to a control obtained from an individual that does not have FSHD, wherein increased expression of the 4q35 gene indicates that the subject is at risk of having or has FSHD.

17. The method of claim 16, wherein the 4q35 gene is FSHD region gene 1 (*FRG1*), FSHD region gene 2 (*FRG2*), or adenine nucleotide translocator-1 gene (*ANT1*).

18. The method of claim 16, wherein the biological sample is from muscle.

19. A non-human transgenic animal one or more of whose cells can overexpress at least one 4q35 gene selected from the group consisting of FSHD region gene 1 (*FRG1*),

FSHD region gene 2 (*FRG2*), or adenine nucleotide translocator-1 gene (*ANT1*), wherein the overexpression of the transgene results in the animal exhibiting symptoms of FSHD.

20. The non-human transgenic animal of claim 19, wherein the 4q35 gene is FRG1.
21. A method of determining whether a treatment for FSHD is effective, the method comprising
 - (a) obtaining a non-human transgenic animal model of FSHD overexpressing a 4q35 gene;
 - (b) administering the treatment to the animal; and
 - (c) evaluating the effect of the treatment on the animal,wherein an improvement in a symptom of FSHD indicates that the FSHD treatment is effective.